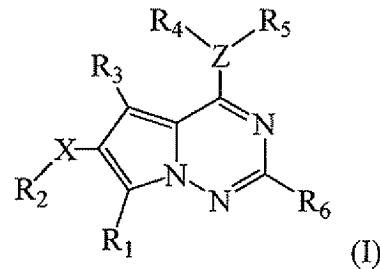


### AMENDMENTS TO THE CLAIMS

Please amend the Claims as follows. Deleted subject matter is indicated in bold text with a strike out and added subject matter is indicated with bold text that is underlined. It is believed that no new matter has been added by any of these changes. This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended) A method of treating one or more conditions associated with p38 kinase activity wherein said conditions are selected from the group consisting of asthma, adult respiratory distress syndrome, chronic obstructive pulmonary disease, chronic pulmonary inflammatory disease, inflammatory bowel disease, osteoporosis, graft vs. host rejection, psoriasis, psoriatic arthritis, traumatic arthritis, rubella arthritis, gouty arthritis and osteoarthritis, comprising administering to a patient in need thereof at least one compound having the formula (I):



or a pharmaceutically acceptable salt, prodrug, or solvate thereof, wherein:

R<sub>3</sub> is hydrogen, methyl, perfluoromethyl, methoxy, halogen, cyano or NH<sub>2</sub>;

X is selected from the group consisting of -O-, -OC(=O)-, -S-, -S(=O)-, -SO<sub>2</sub>-, -C(=O)-, -NR<sub>10</sub>-, -NR<sub>10</sub>C(=O)-, -NR<sub>10</sub>C(=O)NR<sub>11</sub>-, -NR<sub>10</sub>CO<sub>2</sub>-, -NR<sub>10</sub>SO<sub>2</sub>-, -NR<sub>10</sub>SO<sub>2</sub>NR<sub>11</sub>-, -SO<sub>2</sub>NR<sub>10</sub>-, -C(=O)NR<sub>10</sub>-, halogen, nitro, and cyano, or X is absent;

~~Z is selected from O, S, N, and CR<sub>20</sub>, wherein when Z is CR<sub>20</sub>, said carbon atom may form an optionally substituted bicyclic aryl or heteroaryl with R<sub>4</sub> and R<sub>5</sub>;~~

R<sub>1</sub> is selected from the group consisting of hydrogen, -CH<sub>3</sub>, -OH, -OCH<sub>3</sub>, -SH, -SCH<sub>3</sub>, -OC(=O)R<sub>21</sub>, -S(=O)R<sub>22</sub>, -SO<sub>2</sub>R<sub>22</sub>, -SO<sub>2</sub>NR<sub>24</sub>R<sub>25</sub>, -CO<sub>2</sub>R<sub>21</sub>, -C(=O)NR<sub>24</sub>R<sub>25</sub>, -NH<sub>2</sub>, -NR<sub>24</sub>R<sub>25</sub>, -NR<sub>21</sub>SO<sub>2</sub>NR<sub>24</sub>R<sub>25</sub>, -NR<sub>21</sub>SO<sub>2</sub>R<sub>22</sub>,

$-\text{NR}_{24}\text{C}(=\text{O})\text{R}_{25}$ ,  $-\text{NR}_{24}\text{CO}_2\text{R}_{25}$ ,  $-\text{NR}_{21}\text{C}(=\text{O})\text{NR}_{24}\text{R}_{25}$ , halogen, nitro, **or and**  
cyano;

$\text{R}_2$  is selected from **the group consisting of:**

- a) hydrogen, provided that  $\text{R}_2$  is not hydrogen when  $\text{X}$  is  $-\text{S}(=\text{O})-$ ,  $-\text{SO}_2-$ ,  
 $-\text{NR}_{10}\text{CO}_2-$ , or  $-\text{NR}_{10}\text{SO}_2-$ ;
- b) alkyl, alkenyl, and alkynyl optionally substituted with up to four  $\text{R}_{26}$  or  
pentafluoroalkyl;
- c) aryl and heteroaryl optionally substituted with up to three  $\text{R}_{27}$ ; and
- d) heterocyclo and cycloalkyl optionally substituted with keto ( $=\text{O}$ ), up to  
three  $\text{R}_{27}$ , and/or having a carbon-carbon bridge of 3 to 4 carbon atoms; **or and**
- e)  $\text{R}_2$  is absent if  $\text{X}$  is halogen, nitro or cyano;

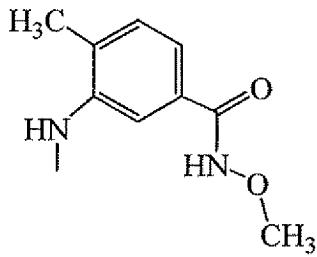
(ii)  ~~$\text{R}_4$  is substituted aryl, aryl substituted with  $\text{NHSO}_2$ alkyl, substituted heteroaryl, an optionally substituted bicyclic 7-11 membered saturated or unsaturated carbocyclic or heterocyclic ring, and~~

~~$\text{R}_5$  is hydrogen, alkyl, or substituted alkyl, except when  $\text{Z}$  is O or S,  $\text{R}_5$  is absent;~~

**or alternatively,**

(ii)  ~~$\text{R}_4$  and  $\text{R}_5$  taken together with  $\text{Z}$  form an optionally substituted bicyclic 7-11 membered aryl or heteroaryl;~~

**the portion  $-\text{Z}(\text{R}_4)(\text{R}_5)$  is selected to be**



R<sub>6</sub> is selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo, -NR<sub>7</sub>R<sub>8</sub>, -OR<sub>7</sub>, **or and** halogen;

R<sub>10</sub> and R<sub>11</sub> are each independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclo, and substituted heterocyclo;

R<sub>7</sub>, R<sub>8</sub>, R<sub>21</sub>, R<sub>24</sub>, and R<sub>25</sub> are each independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, heterocyclo, and substituted heterocyclo;

R<sub>20</sub> is selected from the group consisting of hydrogen, lower alkyl, **or and** substituted alkyl, or R<sub>20</sub> may be absent if the carbon atom to which it is attached together with R<sub>4</sub> and R<sub>5</sub> is part of an unsaturated bicyclic aryl or heteroaryl;

R<sub>22</sub> is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heterocyclo, **or and** substituted heterocyclo;

R<sub>26</sub> is selected from the group consisting of halogen, trifluoromethyl, haloalkoxy, keto (=O), nitro, cyano, -SR<sub>28</sub>, -OR<sub>28</sub>, -NR<sub>28</sub>R<sub>29</sub>, -NR<sub>28</sub>SO<sub>2</sub>, -NR<sub>28</sub>SO<sub>2</sub>R<sub>29</sub>, -SO<sub>2</sub>R<sub>28</sub>, -SO<sub>2</sub>NR<sub>28</sub>R<sub>29</sub>, -CO<sub>2</sub>R<sub>28</sub>, -C(=O)R<sub>28</sub>, -C(=O)NR<sub>28</sub>R<sub>29</sub>, -OC(=O)R<sub>28</sub>, -OC(=O)NR<sub>28</sub>R<sub>29</sub>, -NR<sub>28</sub>C(=O)R<sub>29</sub>, -NR<sub>28</sub>CO<sub>2</sub>R<sub>29</sub>, =N-OH, =N-O-alkyl; aryl optionally substituted with one to three R<sub>27</sub>; cycloalkyl optionally substituted with keto(=O), one to three R<sub>27</sub>, or having a carbon-carbon bridge of 3 to 4 carbon atoms; and heterocyclo optionally substituted with keto (=O), one to three R<sub>27</sub>, or having a carbon-carbon bridge of 3 to 4 carbon atoms; wherein R<sub>28</sub> and R<sub>29</sub> are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, aryl, aralkyl, C<sub>3-7</sub>cycloalkyl, and C<sub>3-7</sub>heterocycle, or may be taken together to form a C<sub>3-7</sub>heterocycle; and wherein each R<sub>28</sub> and R<sub>29</sub> in turn is optionally substituted with up to two members selected from the group consisting of alkyl, alkenyl, halogen, haloalkyl, haloalkoxy, cyano, nitro, amino, hydroxy, alkoxy, alkylthio, phenyl, benzyl, phenoxy, and benzyloxy; and

$R_{27}$  is selected from the group consisting of alkyl,  $R_{32}$ , and  $C_{1-4}$ alkyl substituted with one to three  $R_{32}$ , wherein each  $R_{32}$  group is independently selected from the group consisting of halogen, haloalkyl, haloalkoxy, nitro, cyano,  $-SR_{30}$ ,  $-OR_{30}$ ,  $-NR_{30}R_{31}$ ,  $-NR_{30}SO_2$ ,  $-NR_{30}SO_2R_{31}$ ,  $-SO_2R_{30}$ ,  $-SO_2NR_{30}R_{31}$ ,  $-CO_2R_{30}$ ,  $-C(=O)R_{30}$ ,  $-C(=O)NR_{30}R_{31}$ ,  $-OC(=O)R_{30}$ ,  $-OC(=O)NR_{30}R_{31}$ ,  $-NR_{30}C(=O)R_{31}$ ,  $-NR_{30}CO_2R_{31}$ , and a 3 to 7 membered carbocyclic or heterocyclic ring optionally substituted with alkyl, halogen, hydroxy, alkoxy, haloalkyl, haloalkoxy, nitro, amino, or cyano, wherein  $R_{30}$  and  $R_{31}$  are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, aryl, aralkyl,  $C_{3-7}$ cycloalkyl, and heterocycle, or may be taken together to form a  $C_{3-7}$  heterocycle.

2. (Currently Amended) The method of claim 1 comprising administering to the patient at least one compound ~~having the formula (I), or a pharmaceutically acceptable salt, prodrug or solvate thereof, according to claim 1~~ wherein:

$R_3$  is methyl,  $-CF_3$ , or  $-OCH_3$ ;

$X$  is selected from the group consisting of  $-C(=O)-$ ,  $-NR_{10}-$ ,  $-NR_{10}C(=O)-$ ,  $-NR_{10}CO_2-$ ,  $-NR_{10}SO_2-$ ,  $-SO_2NR_{10}-$ , and  $-C(=O)NR_{10}-$ , or  $X$  is absent;

~~$Z$  is N;~~

$R_2$  is selected from the group consisting of hydrogen,  $C_{2-6}$ alkyl,  $C_{1-4}$ alkyl substituted with up to four  $R_{26}$ , pentafluoroalkyl, ~~or and~~ aryl ~~or and~~ heteroaryl wherein each of the aryl and heteroaryl may optionally be substituted with up to two of  $R_{27}$ ;

~~$R_4$  is phenyl substituted with one  $R_{12}$  and zero to three  $R_{13}$ ;~~

~~$R_5$  and  $R_{10}$  independently are~~ is selected from the group consisting of hydrogen and lower alkyl;

$R_{12}$  is selected from the group consisting of carbamyl, arylsulfonylamine, ~~or and~~ ureido, each of which is optionally substituted with up to two of hydroxy, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, and aralkyl, or alkylsulfonylamine;

$R_{13}$  at each occurrence is independently selected from **the group consisting of** alkyl, substituted alkyl, halo, trifluoromethoxy, trifluoromethyl,  $-OR_{14}$ ,  $-C(=O)alkyl$ ,  $-OC(=O)alkyl$ ,  $-NR_{15}R_{16}$ ,  $-SR_{15}$ ,  $-NO_2$ ,  $-CN$ ,  $-CO_2R_{15}$ ,  $-CONH_2$ ,  $-SO_3H$ ,  $-S(=O)alkyl$ ,  $-S(=O)aryl$ ,  $-NHSO_2-aryl-R_{17}$ ,  $-NHSO_2-alkyl$ ,  $-CONHR_{17}$ , and  $-NHC(=O)NHR_{17}$ ;

$R_{14}$  is hydrogen, alkyl, or aryl;

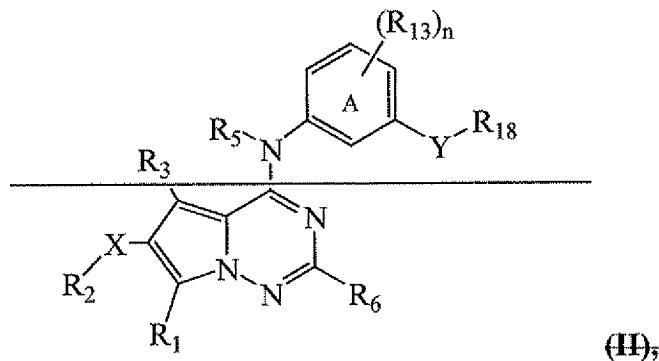
$R_{15}$  is hydrogen or alkyl;

$R_{16}$  is hydrogen, alkyl, aralkyl, or alkanoyl; and

$R_{17}$  is hydrogen, hydroxy, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, or aralkyl.

3. and 4 (Cancel).

5. (Currently Amended) The method of claim **3 2** comprising administering to the patient at least one compound **according to formula (I) having the formula (II):**



or a pharmaceutically acceptable salt, **prodrug**, or **solvate** thereof, wherein:

$R_3$  is methyl or  $CF_3$ ;

$X$  is  $-C(=O)NR_{10}-$ ,  $-NR_{10}C(=O)-$ , or  $-C(=O)-$ ;

$R_1$  is hydrogen,  $-CH_3$ ,  $-OH$ ,  $-OCH_3$ , halogen, nitro, or cyano; **and**

$Y$  is  **$C(=O)NH$** ,  **$NHC(=O)NH$** , or  **$NHSO_2$** ;

$R_{10}$  is hydrogen or lower alkyl ;

~~R<sub>18</sub> is selected from hydrogen, alkyl, alkoxy, aryl, and aryl substituted with one to three R<sub>19</sub>, except that when Y is -NHSO<sub>2</sub>-, R<sub>18</sub> is C<sub>1-4</sub>alkyl, aryl or aryl substituted with R<sub>19</sub>;~~

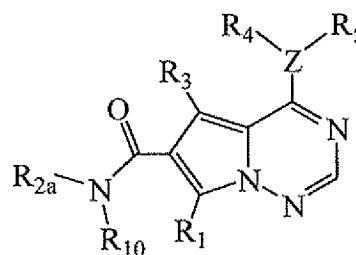
$R_{13}$  is attached to any available carbon atom of phenyl ring A and at each occurrence is independently selected from alkyl, substituted alkyl, halo, trifluoromethoxy, trifluoromethyl,  $-OR_{14}$ ,  $-C(=O)alkyl$ ,  $-OC(=O)alkyl$ ,  $-NR_{15}R_{16}$ ,  $-SR_{15}$ ,  $-NO_2$ ,  $-CN$ ,  $-CO_2R_{15}$ ,  $-CONH_2$ ,  $-SO_3H$ ,  $-S(=O)alkyl$ ,  $-S(=O)aryl$ ,  $-NHSO_2-aryl-R_{17}$ ,  $-NHSO_2C_{1-4}alkyl$ ,  $-CONHR_{17}$ , and  $-NHC(=O)NHR_{17}$ .

**R<sub>14</sub>, R<sub>15</sub>, R<sub>16</sub> and R<sub>17</sub> are hydrogen or alkyl;**

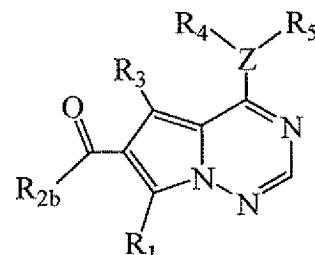
**R<sub>19</sub>** at each occurrence is selected from alkyl, halo, trifluoromethoxy, trifluoromethyl, hydroxy, alkoxy, alkanoyl, alkanoyloxy, thiol, alkylthio, ureido, nitro, cyano, carboxy, carboxyalkyl, carbamyl, alkoxy carbonyl, alkylthieno, arylthieno, arylsulfonyl amine, sulfonic acid, alkysulfonyl, sulfonamido, and aryloxy, wherein each group **R<sub>19</sub>** may be further substituted by hydroxy, alkyl, alkoxy, aryl, or aralkyl; and

~~n is 0, 1 or 2.~~

6. (Currently Amended) The method of claim 3 2, comprising administering to the patient at least one compound having the formula **I** wherein  $R_2$  is selected from the group consisting of  $N(R_{2a})(R_{10})$  and  $R_{2b}$  to give compounds of formula (Ia) or (Ib):



(1a)



(Ib)

or a pharmaceutically acceptable salt, ~~prodrug or solvate~~ thereof, wherein:

R<sub>3</sub> is methyl or CF<sub>3</sub>;

$R_{2a}$  and  $R_{2c}$  are each independently selected from the group consisting of hydrogen,

$C_{2-6}$ alkyl, substituted  $C_{1-4}$ alkyl, aryl, substituted aryl, benzyl, and substituted benzyl;  
 $R_{2b}$  is heterocyclo or substituted heterocycle; and  
 $R_{10}$  is hydrogen or lower alkyl.

7. to 11 (Previously cancelled).